ELSEVIER

Blood 142 (2023) 1160–1161

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

201.GRANULOCYTES, MONOCYTES, AND MACROPHAGES

Mavorixafor for Patients with Chronic Neutropenic Disorders Treated with G-CSF: Preliminary Response Data and G-CSF Dose Reduction in an Ongoing Phase 2, Open-Label, Multicenter Study Support Reduction in G-CSF Dosing

Julia T. Warren, MDPhD[1,2], Kathryn E. Dickerson, MDMS[3], Anjali A. Sharathkumar, MBBS, MD MS[4], Jolan E. Walter, MD PhD[5], David B. Wilson, MD PhD[6], Katrina P. Adell, MD[7], Kelly Chen, PhD[7], Susan Dubuc, RN, MSN[7], Rick MacLeod[7], Katie Peters, MS[7], Murray Stewart, MD[7], Arthur G. Taveras, PhD[7], Kelly Walkovich, MD[8]

[1] Division of Hematology, Children's Hospital of Philadelphia, Philadelphia, PA
[2] Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
[3] Division of Hematology & Oncology, Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX
[4] Stead Family Department of Pediatrics, Carver College of Medicine, University of Iowa Health Care, Iowa City, IA
[5] Division of Allergy & Immunology, Department of Pediatrics, Morsani College of Medicine, University of South Florida at Johns Hopkins All Children's Hospital, St. Petersburg, FL
[6] Department of Pediatrics, Washington University School of Medicine, St. Louis, MO
[7] X4 Pharmaceuticals, Inc., Boston, MA
[8] C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, MI

Introduction: Chronic neutropenia (CN) encompasses multiple disorders characterized by an absolute neutrophil count (ANC) <1500 cells/μL for >3 months, leading to increased susceptibility to recurrent and/or severe infections. CN can be sub-classified as congenital neutropenia defined by genetic variants (*ELANE* variants are the most common), cyclic neutropenia (CyN) supported by documentation of ANC cycling with reciprocal monocytosis most often associated with certain *ELANE* variants, or chronic idiopathic neutropenia (CIN) defined as acquired neutropenia without an identifiable cause. The current treatment approach for CN involves long-term use of injectable granulocyte colony-stimulating factor (G-CSF), which can have associated adverse events (AEs) [Donadieu J. *Expert Rev Hematol*. 2021; Fioredda F. *Hemasphere*. 2023; Newburger PE. *Semin Hematol*. 2013]. Therefore, efforts are under way to discover other therapies for CN. In a phase 3 trial (NCT03995108), mavorixafor, an investigational oral CXCR4 antagonist, showed durable increases in ANC and reduction in total infection rate and severity in people with WHIM (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis) syndrome [Badolato R. *Clin Immunol*. 2023]. Mavorixafor is being studied in a phase 2 trial for chronic neutropenic disorders (NCT04154488) [Warren JT. *Blood*. 2022] to evaluate the durability, safety, and tolerability of chronic dosing of mavorixafor with or without concurrent G-CSF. Here, we describe preliminary results for 3 participants in the ongoing phase 2 trial.
Methods: Individuals (aged ≥12 years) with diagnosis of congenital neutropenia, CyN, or CIN ≥6 months prior and ANC <1000/μL (or no lower limit but <10,000/μL if on G-CSF) at screening visits were enrolled in the phase 2 trial. Eligible adult participants received once-daily 400 mg of mavorixafor while adolescents received weight-based dosing (>50 kg, 400mg; ≤50 kg, 200 mg) for 6 months with or without G-CSF. Participants already on G-CSF continued their individualized G-CSF dosing for ≥8 weeks, followed by potential dose and/or frequency reduction based on monthly ANC assessments. Hematologic parameters, including ANC, were assessed over 8 hours on day 1 and at months 1 and 3, with continued assessment at month 6. At months 2 and 4 (assessment to continue at month 5), hematologic parameters were assessed within 2 to 4 hours of dosing to reduce trial burden.
Results: Data are reported as of July 17, 2023. Preliminary data from the first 3 participants on G-CSF receiving chronic once-daily oral mavorixafor for at least 2 months showed increases in mean ANC compared with baseline (BL) at all time points assessed in all participants. ANCs reached normal ranges for all participants. Increases in ANC supported physicians' decisions to reduce G-CSF dosing.
Two participants (P1 and P2) with CIN achieved increases in ANC that enabled initiation of G-CSF tapering at month 2. For P1, G-CSF dose was tapered to 50% at month 2, and further G-CSF tapering occurred at month 3. ANC remained within normal ranges during this period. At month 4, G-CSF dosing was fully withdrawn, and the participant continued daily mavorixafor monotherapy. For P2, ANC increased ~3x baseline by month 2. G-CSF dose was tapered to 50% after month 2. ANC remained

within normal ranges during this period. At month 3, G-CSF dosing was fully withdrawn, and the participant continued daily mavorixafor monotherapy with an ANC ˜1000 cells/μL.
A third participant (P3) with CyN receiving mavorixafor daily with concurrent G-CSF showed increases in ANC over BL for 4 months.
All 3 participants remain on study, and have not experienced any serious AEs
Conclusions: Our report shows that chronic treatment with oral, once-daily mavorixafor in combination with G-CSF resulted in durable increases in ANC compared with BL for ≥3 months in 3 study participants. Reduction of injectable G-CSF dosing was implemented in 2 study participants with CIN following robust ANC increase observed after the first 2 months of combination treatment. These preliminary data also support the safety of concomitant treatment with G-CSF and mavorixafor. Additional data from the ongoing phase 2 study will further elucidate the potential of daily, oral mavorixafor as a treatment for CN to reduce the burden and associated AEs of injectable G-CSF. A phase 3 trial of people with CN is being planned.

Disclosures Warren: *X4 Pharmaceuticals:* Consultancy, Research Funding. **Dickerson:** *Agios:* Membership on an entity's Board of Directors or advisory committees. **Sharathkumar:** *Spark Therapeutics:* Consultancy; *Genentech:* Consultancy; *Amgen:* Research Funding. **Walter:** *Chiesi:* Research Funding; *MustangBio:* Research Funding; *Octapharma:* Research Funding; *Novartis:* Research Funding; *Bristol-Myers Squibb:* Research Funding; *Janssen:* Research Funding; *Pharming:* Consultancy, Speakers Bureau; *Regeneron:* Consultancy, Research Funding; *Enzyvant:* Consultancy; *ADMA Biologicals:* Consultancy, Research Funding; *Grifols:* Consultancy; *CSL-Behring:* Consultancy; *X4 Pharmaceuticals Inc.:* Consultancy, Research Funding; *Takeda:* Consultancy, Research Funding, Speakers Bureau. **Adell:** *X4 Pharmaceuticals Inc.:* Current Employment; *EpimAb Biotherapeutics:* Ended employment in the past 24 months. **Chen:** *X4 Pharmaceuticals Inc.:* Current Employment. **Dubuc:** *X4 Pharmaceuticals, Inc.:* Current Employment, Divested equity in a private or publicly-traded company in the past 24 months. **MacLeod:** *X4 Pharmaceuticals Inc.:* Current Employment. **Peters:** *X4 Pharmaceuticals Inc.:* Current Employment. **Stewart:** *X4 Pharmaceuticals Inc.:* Current Employment, Current equity holder in publicly-traded company. **Taveras:** *X4 Pharmaceuticals, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Walkovich:** *AstraZeneca:* Membership on an entity's Board of Directors or advisory committees; *Sobi:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pharming:* Membership on an entity's Board of Directors or advisory committees; *Horizon:* Membership on an entity's Board of Directors or advisory committees; *UpToDate:* Patents & Royalties: Royalties from UpToDate; *American Society of Hematology:* Honoraria; *St. Jude:* Honoraria; *X4 Pharmaceuticals, Inc.:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *NICER:* Other: NICER Consortium, Executive Chair .

https://doi.org/10.1182/blood-2023-173549